RWLP0203

ARTICLE

Passive Cigarette Smoke Exposure of Infants

Importance of Nonparental Sources

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Objective: To learn whether cigarette smoking by persons other than parents significantly contributes to the passive environmental tobacco smoke (ETS) exposure of infants.

Study Design: A cohort of infants prospectively followed up from birth to age 2 years with monthly questionnaires concerning smoking by different categories of adults coming into contact with the infants.

Setting: Health maintenance organization members residing in several suburban communities of Detroit, Mich, defined by contiguous ZIP codes.

Subjects: Ninety-seven (83%) of 117 healthy, full-term infants, thought to be at high risk of allergic disease based on cord blood IgE, who were born to eligible mothers and who completed 24 months of follow-up.

Main Outcome Measures: Average of bimonthly urinary cotinine-creatinine ratios (CCRs) during the 2 years of the study.

Results: There were significant correlations ($r \geq 0.28$, $P \leq .005$) between the frequency of smoking by all 7 categories of adults considered and the average CCRs of the infants. Multivariable analysis demonstrated that average urinary CCRs were significantly associated not only with smoking by the infant's parents, but also with smoking by workers at day care away from the home, persons visited away from the home, and persons other than parents residing in the home (overall $R^2 = 0.72$, $P = .001$).

Conclusions: Smoking by multiple individuals, other than the parents, significantly contributes to the ETS exposure of infants. These findings suggest that, at least for infants, efforts to reduce the adverse health effects of ETS exposure should extend beyond curtailing parental smoking.

Arch Pediatr Adolesc Med. 2000;154:1237-1241

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NUMEROUS investigations have demonstrated adverse health effects from passive exposure to environmental tobacco smoke (ETS) in both adults and children. Major adverse effects of ETS exposure in infants and children include an increased frequency of lower respiratory tract illness, asthma, otitis media, hospitalization, and sudden infant death syndrome.[1-10]

Maternal smoking has been the primary and sometimes the only source of ETS exposure related to adverse health effects in children.[3,7,10-12] Other sources of potential ETS exposure, such as from fathers, day care workers, visitors in the child's home, and residents of the child's home other than parents, were either considered statistically insignificant or were not evaluated.[8-12] Estimates of a child's ETS exposure from questionnaire information concerning smoking by parents and others may be imprecise for several reasons. Smoking near a child may be underreported or overreported because of guilt feelings, lapses in memory, or inaccurate estimates of the frequency of smoking. The relationship of questionnaire data to actual ETS exposure may also be imprecise because of many variables that are not normally considered, such as the distance between a smoker and the child, room size, room ventilation, and the child's minute ventilation.[13-16] One method of attempting to overcome these difficulties is by measuring a biomarker of ETS absorption. A frequently used biomarker of nicotine absorption is cotinine measured in blood, saliva, or urine.[7,13,17,18] Cotinine is a relatively specific metabolite of nicotine and, because of its longer half-life in comparison with nicotine, cotinine concentrations are a reflection of nicotine absorption during the preceding 24 to 72 hours.[7,19,20]

As part of a prospective, longitudinal study concerning the development of

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SUBJECTS AND METHODS

SUBJECTS

The selection of the study cohort has been previously described.[21] Briefly, all pregnant women living in an area of northern suburban Detroit, Mich, defined by contiguous ZIP codes and belonging to the largest health maintenance organization in Michigan, were eligible for recruitment if their infants were due between April 15, 1987, and August 31, 1989. Women meeting eligibility criteria were invited to participate during prenatal visits. If the woman agreed to participate, written informed consent, demographic data, and health- and lifestyle-related data, including smoking habits, were collected by a study nurse. The parents of newborns thought to be at increased risk of allergic disease, based on cord blood IgE concentrations of ≥0.56 IU/mL, were asked to allow their child to participate in an intensive follow-up study. All aspects of the study were approved by the Henry Ford Hospital Human Rights Committee (Detroit) and written informed consent was obtained from the parents at appropriate times.

A study nurse made monthly home visits to participating families and collected information about the infant's exposure to smokers including parents or guardians, persons providing day care both in the home and outside the home, persons visiting the home more than 2 hours per week, and persons visited away from the home for more than 2 hours (eg, family friends and relatives). An attempt was made to obtain a urine specimen every second month for measurement of cotinine and creatinine. Data from birth through age 2 years are included in this study. Cotinine levels in the urine were measured by radioimmunoassay by the Clinical Biochemistry Facility, American Health Foundation (Valhalla, NY). Creatine levels were also measured to correct for the dilution of the urine. In an effort to correct for the wide variation in urine specific gravities, all analyses are performed using the cotinine-creatinine ratio (CCR), expressed as nanograms of cotinine per milligram of creatinine, as in other studies.[7,16,17]

STATISTICAL METHODS

During data analysis the natural logarithmic transformation of the CCR +1 (LnCCR) was used so that the distribution of the data more closely approximated a normal distribution. One was added to each CCR to avoid the mathematically undefined quantity of the logarithm of 0.

Seven variables, categorizing the frequency of smoking by groups of persons potentially coming into close contact with the infants, were generated based on the questionnaire results. These were defined as the percentage of times the questionnaire identified potential ETS exposure as a result of smoking by an individual included in the group. The questionnaire was administered monthly over 2 years so each exposure variable represents the average of up to 24 observations. At least 3 observations were required for inclusion in this analysis. The 7 groups of individuals were (1) mothers or female guardians, (2) fathers or male guardians, (3) other regular residents of the child's home, (4) persons visiting the home for more than 2 hours per week (other than day care), (5) persons the infant visited outside the home for more than 2 hours (other than day care), (6) persons providing day care inside the home, and (7) persons providing day care outside of the home. Variables representing smoking by persons within groups over 2 years were expressed as fractions ranging from 0, indicating that no smoking was ever reported by any member of the group, to 1, indicating that smoking was always reported by at least 1 member of the group on each questionnaire. A summary estimate of the total potential ETS exposure during the 2 years of observation was generated by adding the fractions indicating smoking for each of the 7 groups.

The smoke exposure variables were correlated to the average LnCCR+1 for the infants using Pearson correlation. A multiple regression approach was used to assess which sets of variables best predicted the average LnCCR of the infants. A stepwise technique was used for the individual variables followed by evaluation of particular a priori interactions of interest. $P<.05$ was considered an indication of statistical significance.

allergic disease in children, we collected questionnaire information about possible sources of ETS exposure and urine samples for cotinine measurements in a birth cohort of infants followed up from birth until age 2 years. The data were analyzed to determine the relative contributions from different groups of cigarette smokers to the average urinary cotinine concentration in the infants. We specifically wanted to learn whether the mother's smoking was the dominant determinant of an infant's ETS exposure and whether smoking by others in the vicinity of the infant significantly contributed to ETS exposure.

RESULTS

One hundred seven of 117 eligible infants were initially enrolled in the study; 8 families dropped out within the first 6 months, leaving 99 infants. Each child was scheduled to have 12 urine samples, one every other month for 2 years, and 24 monthly questionnaires. There were 97 infants (98%) who had at least 3 urine samples and 6 questionnaires completed. For these 97 infants a total of 703 (60.4%) of the scheduled urine samples and 2115 (90.9%) of the questionnaires were completed for an average of 7.2 and 21.8 per child, respectively. Of the 97 participating infants, 90 (92.8%) were white, 1 (1.0%) was African American, and 6 (6.2%) were from other racial groups. Consistent with the fact that these children were from middle-class suburbs, 73.1% of the fathers had at least some college education as did 71.1% of the mothers.

The reported smoking habits of the mothers and fathers were generally consistent throughout the 2-year observation period, although there were occasional changes in smoking habits. Considering these occasional changes, we arbitrarily defined nonsmokers as those who reported smoking on less than 25% of the questionnaires and smokers as those who reported smoking on 25% or more of the questionnaires. Of the 97 mothers, 78 were classified as nonsmokers and 19 as smokers. None of the mothers who smoked during pregnancy stopped smoking during the study and 4 women who had stopped smoking during pregnancy started again before the infant was 1 month of age and continued throughout the

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Table 1. Correlations Between Reported Smoking Frequency and Average Log-Transformed Cotinine-Creatinine Ratios

Group*	Smoking Frequency, %†	Correlation	P
Mothers or female guardians	9.0	0.66	.001
Fathers or male guardians	22.3	0.62	.001
Day care in the home	5.5	0.53	.001
Persons visited away from home	33.6	0.48	.001
Day care away from the home	12.1	0.36	.001
Other people living in the home	6.2	0.30	.003
Visitors to the home	20.7	0.28	.005

*For each group, any reported smoking by any member of the group is considered smoking by the group.
†Smoking by person providing day care for the infant either in the infant's home or in a location other than the infant's home.

2 years of the study. Seventy-two fathers were nonsmokers and 25 were smokers. Overall, mothers and fathers classified as nonsmokers reported smoking on only 0.2% of questionnaires. Reports of mothers and fathers classified as smokers were less consistent. Five of 19 smoking mothers and 11 of 25 smoking fathers were reported as nonsmokers at least once; however, mothers classified as smokers reported smoking on 95.8% of all questionnaires and fathers classified as smokers reported smoking on 88.0% of all questionnaires. The reported smoking status of other groups considered in this study was much less consistent (data not shown).

In the study population of 97 infants, CCRs ranged from 0 to 5300 ng/mg. The average of the mean CCRs for all infants was 250 ng/mg (SD=503 ng/mg) compared with averages of 94 ng/mg (SD=165 ng/mg) for infants of nonsmoking mothers and 890 ng/mg (SD=833 ng/mg) for infants of smoking mothers.

To evaluate the relationships between reported smoking and average CCRs, we first examined the correlations between the mean percentage of the time smoking was reported by each of the 7 groups of persons to whom the infant might be exposed, and the mean LnCCR for the infant. The results of these calculations are presented in **Table 1**. The mothers' and fathers' smoking frequencies have the highest correlations with the mean CCRs for infants: 0.66 and 0.62, respectively. The smoking frequencies for day care, when it is provided in the home, and smoking by persons visited away from home, have similar correlations, with average CCRs of 0.53 and 0.48, respectively. The correlations between average CCRs and smoking frequency of day care away from the home (0.36), other residents at the child's home (0.30), and visitors to the child's home (0.28) are smaller but still highly significant.

Multiple regression modeling was used to evaluate the relationships between questionnaire data about potential ETS exposures and an infant's mean CCR. The final multiple regression model is presented in **Table 2**. The model shows that the frequency of smoking by mothers, fathers, persons visited away from home, other persons living in the home, and child care away from home are all significant contributors to the average CCRs found in the infants. The overall model for predicting the average LnCCR has a high R^2 of 0.72 and is significant with

Table 2. Summary of Multiple Regression Model* for Predicting the Logarithm of an Infant's Average Cotinine-Creatinine Ratio

Variable	Coefficient	SE	P
Intercept	1.84	0.25	.001
Mother's smoking frequency	2.69	0.51	.001
Father's smoking frequency	2.36	0.40	.001
Mother × father interaction	−1.25	0.74	.09
Smoking frequency of persons visited away from home	1.75	0.39	.004
Smoking frequency of other people in home	1.64	0.59	.007
Smoking frequency of persons providing child care away from home	2.76	0.80	.001
Child's sex† × child care away from home interaction	−1.93	1.07	.08
Child's sex†	−0.24	0.26	.35

*Overall R^2 = 0.72 with model P = .001.
†Child's sex is coded 0 for male and 1 for female.

P=.001. Two interactions were included in the model based on P values of less than .10, a level we considered significant for interactions. The first is an interaction between maternal and paternal smoking. The mothers' smoking frequency and fathers' smoking frequency have similar coefficients of 2.7 and 2.4, respectively. The negative coefficient for the mother-father interaction suggests that the 2 exposure sources are not additive. Compared with no smoke exposure, a mother's smoking alone increases the LnCCR by 2.7, while the father's smoking alone increases the LnCCR by 2.4, but when both the mother and father smoke the LnCCR increases to only 3.8 (not 2.7 + 2.4 or 5.1 as would be predicted by an additive effect). The second interaction is between the child's sex and day care. Reported smoke exposure during day care away from the home (coefficient=2.76) and the interaction between this exposure category and the infant's sex (coefficient=−1.93) are both significant in the model. The sex of the infant (coefficient=−0.24) as a individual variable was not significant but was included in the model for completeness. These coefficients imply that for male children, ETS exposure in day care away from home increases the LnCCR by 2.76, while for female children, similar exposure increases LnCCRs by only 0.59, since the variable for the infants' sex entered into the model was coded as 1 for males and 0 for females. We examined the condition indices to check for multicollinearity in this regression model and found that all indices were well below the levels suggesting collinearity.[22]

To further evaluate the relationship between the 2-year mean CCRs and all potential sources of ETS exposure reported during the same interval, we compared the mean LnCCRs of each infant to the sum of the fractions of the time smoking was reported for each of the 7 previously defined groups of people. If smoking was never reported by any member of the groups around an infant during the 2 years, the sum would be 0, while if smoking was always reported for at least 1 individual in each group the sum would be 7. The results of this analysis

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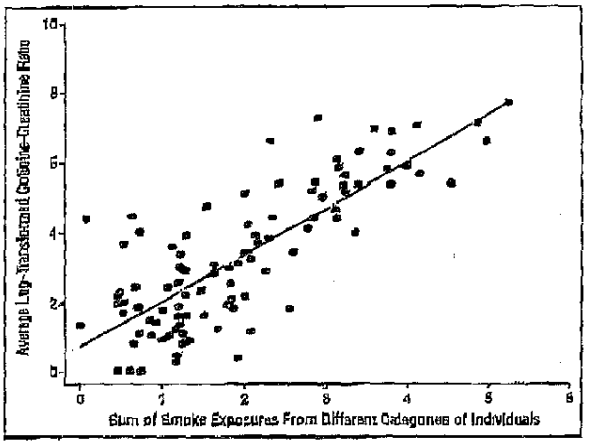

Correlation between the sum of the percentages of time that infants were reportedly exposed to environmental tobacco smoke from 7 different groups of individuals and the logarithmically transformed average of all of the cotinine-creatinine ratios for the infants. The correlation coefficient for the 97 infants studied is highly significant (r=0.80, P<.001).

are shown in the **Figure**. The correlation of 0.80 is highly significant (P<.001) and appears to be linear, suggesting that as the frequency of smoking by individuals coming into contact with an infant increases, the mean LnCCR of the infant increases proportionally. If parental smoking was the dominant source of exposure the curve would be expected to increase from 0 to 2 and then flatten or be random between 2 and 6.

We also looked at the average CCRs in infants when both parents were nonsmokers. A previous study found that a CCR of more than 30 ng/mg differentiated ETS-exposed from nonexposed children.[18] Using this value we found that 31 (47.7%) of the 65 infants of nonsmoking parents had average CCRs of more than 30 ng/mg. The average CCR for these 31 children was 97.9 ng/mg. Among these 65 infants of nonsmoking parents, only 6 (25.0%) of 24 infants who were reported as exposed to either none or 1 category of smoking adult had average CCRs of greater than 30 ng/mg, but 25 (61.0%) of the 41 infants exposed to 2 or more categories of smoking adults had average CCRs of more than 30 ng/mg.

COMMENT

We have found that smoking by adults other than parents was significantly related to the average ETS exposure of infants as assessed by urinary CCRs between birth and age 2 years. In many infants exposure to ETS from adults other than the parents produced CCRs that were above the previously reported threshold used to identify children of smoking parents.[18] Given the many adverse health effects related to passive ETS exposure, our results suggest that the safety of infants depends on reducing smoking by all adults having regular contact with infants, not just the parents.

Our results are generally consistent with previous studies. The CCRs we observed are similar to those reported by others.[7,18,23] Given the many variables related to ETS exposure, the relative large variations we observed in CCRs within infants during 2 years of observation is understandable. While some have suggested that cotinine measurements are relatively stable over time in passively exposed children,[18,24] others have also reported large variations.[16]

We were not surprised to find that self-reported smoking was very consistent in this group of suburban parents. Even though their child was enrolled in a study evaluating factors associated with the development of allergic disease, few parents stopped smoking during the 2 years of observation. Our observation that smoking by other groups was less consistent than parental smoking is understandable, since multiple individuals were often considered together in the other groups; eg, visitors to the infant's home could be a family friend one day and a grandparent another day. Consistent with other studies, we found a highly significant correlation between maternal smoking and the quantity of cotinine in an infant's urine.[15,17,18,25,26] Also consistent with some other studies,[7,15,24,25] we found that smoking by other adults was significantly correlated with urinary cotinine measurements.

We were surprised to find that a noticeable proportion of children with nonsmoking parents showed evidence of relatively high levels of ETS exposure. This discrepancy shows the value of either using a biomarker of ETS exposure or collecting comprehensive exposure data, rather than relying solely on reports of parental smoking as an estimate of ETS exposure. As we have previously reported, repeated measurements of urinary CCRs vary widely for individual infants.[16] This variability from one sample to another suggests that cross-sectional studies of ETS exposure based on CCRs must be interpreted cautiously. However, the average of multiple CCRs, obtained during 2 years of observation, was highly correlated with the estimated frequency of ETS exposure reported on detailed questionnaires.[16]

Strengths of this study include the prospective design, the relatively large number of infants, and the repeated sampling with both questionnaires and CCR measurements. The relatively high retention rate of infants and the fraction of samples actually completed are also important. The urinary cotinine and creatinine values were measured in an experienced laboratory, in a blinded fashion, using standard methods, reducing the risk of laboratory bias.

One limitation of our study is that we only asked about whether adults in each group smoked and did not ask about the number of cigarettes smoked. If we had obtained data on the amount each person smoked we might have found an even stronger correlation between the questionnaires and CCR measures. Another limitation is the failure to obtain all of the scheduled urine samples and to complete follow-up of all infants originally enrolled in the study. We do not feel that these are likely to have resulted in erroneous results since the number of dropouts was small and we obtained more than 60% of the scheduled urine samples, an average of more than 7 of the 12 scheduled urine samples per child. It would have been better to obtain monthly or bimonthly serum samples for cotinine analysis; however, this was not feasible.

We did not attempt to analyze the data for changes in CCRs with increasing age, since the age interval we studied was small and we expected that most infants of

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this age would be kept in relatively close proximity to parents. We did analyze our data to see if there was evidence that breastfeeding by a smoking mother increased the CCR in her infant. We found evidence that nicotine or cotinine was transmitted by breastfeeding, in that breastfed infants of smoking mothers had higher CCRs than bottle-fed infants of smoking mothers. We did not present these data here, since others have already done so and this finding does not alter our other conclusions.[27,28]

In conclusion, we have found that smoking by many adults beyond an infant's parents significantly contributes to the average quantity of cotinine found in the urine of infants. Given the many well-documented adverse effects of passive ETS exposure, our findings suggest that efforts to reduce the health effects of ETS on infants must include reducing exposure to all sources of cigarette smoke.

Accepted for publication July 27, 2000.

This study was supported by grant AI24156 from the National Institutes of Allergy and Infectious Diseases, Bethesda, Md, grant P03ES06639 from the Fund for Henry Ford Hospital, Detroit, Mich, and the National Institute of Environmental Health Sciences Center, Research Triangle Park, NC.

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REFERENCES

1. Kraemer MJ, Richardson MA, Weiss NS, et al. Risk factors for persistent middle-ear effusions: otitis media, catarrh, cigarette smoke exposure and atopy. *JAMA*. 1983;249:1022-1025.
2. Ey JL, Holberg CJ, Aldous MB, et al. Passive smoke exposure and otitis media in the first year of life. *Pediatrics*. 1995;95:670-677.
3. Schoendorf KC, Kiely JL. Relationship of sudden infant death syndrome of maternal smoking during and after pregnancy. *Pediatrics*. 1992;90:905-908.
4. Kahn A, Groswasser J, Sottiaux M, et al. Prenatal exposure to cigarettes in infants with obstructive sleep apneas. *Pediatrics*. 1994;93:778-783.
5. Gortmaker SL, Walker DK, Jacobs FH, Ruch-Ross H. Parental smoking and the risk of childhood asthma. *Am J Public Health*. 1982;72:574-579.
6. Pedreira FA, Guandolo VL, Feroli EJ, Malia GW, Weiss IP. Involuntary smoking and incidence of respiratory illness during the first year of life. *Pediatrics*. 1985; 75:594-597.
7. Ehrlich R, Kattan M, Godbold J, et al. Childhood asthma and passive smoking: urinary cotinine as a biomarker of exposure. *Am Rev Respir Dis*. 1992;146:544-599.
8. Murray AB, Morrison BJ. Passive smoking by asthmatics: its greater effect on boys than on girls and on older than on younger children. *Pediatrics*. 1989;84: 451-459.
9. Martinez FD, Cline M, Burrows B. Increased incidence of asthma in children of smoking mothers. *Pediatrics*. 1992;89:21-26.
10. Weitzman M, Gortmaker S, Walker DK, Sobol A. Maternal smoking and childhood asthma. *Pediatrics*. 1990;85:505-511.
11. Tager IB, Weiss ST, Muñoz A, Rosner B, Speizer FE. Longitudinal study of the effects of maternal smoking on pulmonary function in children. *N Engl J Med*. 1983;309:699-703.
12. Wright AL, Holberg C, Martinez FD, Taussig LM. Relationship of parental smoking to wheezing and nonwheezing lower respiratory tract illnesses in infancy. *J Pediatr*. 1991;118:207-214.
13. Jarvis MJ, Russell MAH. Measurement and estimation of smoke dosage in non-smokers from environmental tobacco smoke. *Eur J Respir Dis*. 1982;65:68-75.
14. Delilkan RJ, Ernst P, Jaakkola MS, Solomon S, Becklake MR. Questionnaire assessments of recent exposure to environmental tobacco smoke in relation to salivary cotinine. *Eur Respir J*. 1993;6:1104-1108.
15. Coultas DB, Howard CA, Peake GT, Skipper BJ, Samet JM. Salivary cotinine levels and involuntary tobacco smoke exposure in children and adults in New Mexico. *Am Rev Respir Dis*. 1987;136:305-309.
16. Coultas DB, Samet JM, McCarthy JF, Spengler JD. Variability of measures of exposure to environmental tobacco smoke in the home. *Am Rev Respir Dis*. 1990; 142:602-606.
17. Greenberg RA, Haley NJ, Etzel RA, Loda FA. Measuring the exposure of infants to tobacco smoke: nicotine and cotinine in urine and saliva. *N Engl J Med*. 1984; 310:1075-1078.
18. Henderson FW, Reid HF, Morris R, et al. Home air nicotine levels and urinary cotinine excretion in preschool children. *Am Rev Respir Dis*. 1988;140:197-201.
19. Benowitz NL, Kyut F, Jacob P, Jones RT, Osman AL. Cotinine disposition and effects. *Clin Pharmacol Ther*. 1983;34:604-611.
20. Benowitz NL, Jacob P. Nicotine and cotinine elimination pharmacokinetics in smokers and nonsmokers. *Clin Pharmacol Ther*. 1993;53:316-323.
21. Ownby DR, Johnson CC, Peterson EL. Maternal smoking does not influence cord serum IgE or IgD concentrations. *J Allergy Clin Immunol*. 1991;88:555-560.
22. Belsley DA, Kuh E, Welsch RE. *Regression Diagnostics: Identifying Influential Data and Sources of Collinearity*. New York, NY: Wiley & Sons; 1980:112.
23. Reese AC, James IR, Landau LI, Lescuit PM. Relationship between urinary cotinine level and diagnosis in children admitted to hospital. *Am Rev Respir Dis*. 1992;146:66-70.
24. Jarvis MJ, Martelli AD, Russell MAH, West RJ, Bryant A, Feyerabend C. Passive smoking in adolescents: one-year stability of exposure in the home. *Lancet*. 1987; 2:1324-1325.
25. Willers S, Svanonius E, Skarping G. Passive smoking and childhood asthma. *Allergy*. 1991;46:330-334.
26. Peterson EL, Johnson CC, Ownby DR. Use of urinary cotinine and questionnaires in the evaluation of infant exposure to tobacco smoke in epidemiologic studies. *J Clin Epidemiol*. 1997;50:917-923.
27. Schulte-Hobein B, Schwartz-Bickenbach D, Abt S, Plum C, Nau H. Cigarette smoke exposure and development of infants throughout the first year of life: influence of passive smoking and nursing on cotinine levels in breast milk and infant's urine. *Acta Paediatr Scand*. 1992;81:550-557.
28. Klonoff-Cohen HS, Edelstein SL, Lefkowitz ES, et al. The effect of passive smoking and tobacco exposure through breast milk on sudden infant death syndrome. *JAMA*. 1995;273:795-798.

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